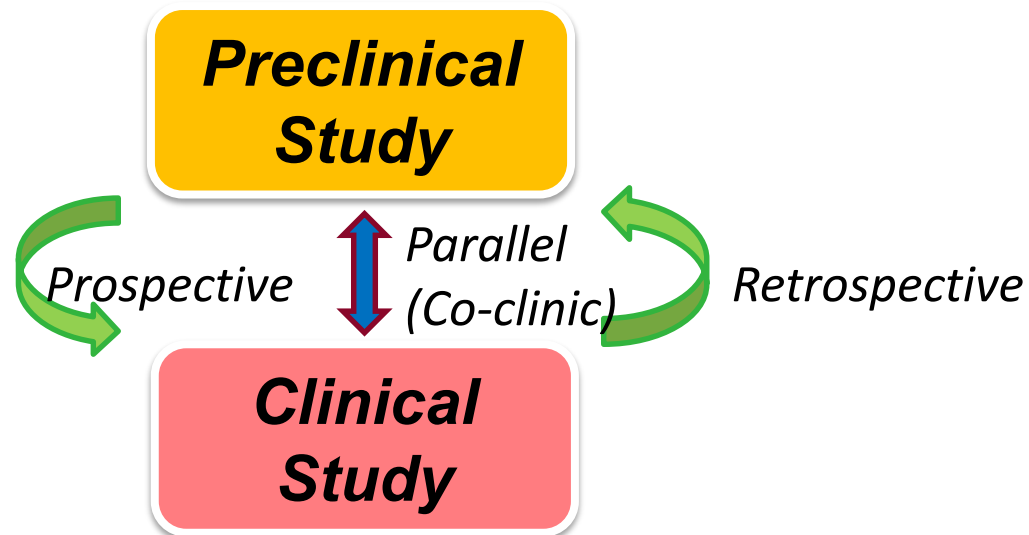


Promise and Challenges of Co-Clinical Imaging

Huiming Zhang, Ph.D., Cancer Imaging Program, DCTD, NCI

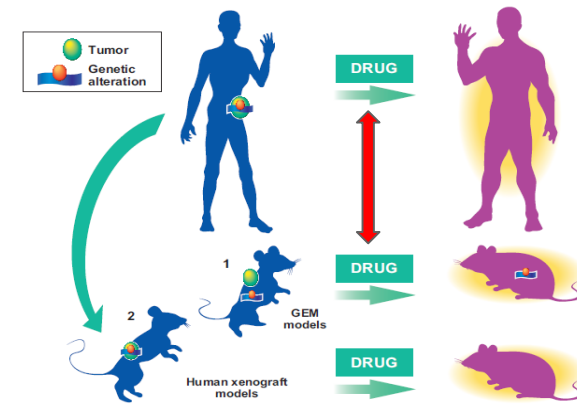
Rationale

- ❑ Precision medicine requires better animal models & novel research,
- ❑ Preclinical study is linked to clinic study via multiple pathways,
- ❑ Quantitative imaging (QI) as a non-invasive tool.



Background

Co-clinical trials: investigations in patients and in parallel (or sequential) in mouse or human-in-mouse models (GEMMs or PDXs) of cancer that mirror the genetic and biology of the patients malignancies or precancerous lesions.



Nardella et al, Cancer Discovery 2011:1:108

Progresses:

2009: NCI U01s: *Integration of Mouse Models into Human Cancer Research*,

2012: first co-clinical trial report on NSCLC,

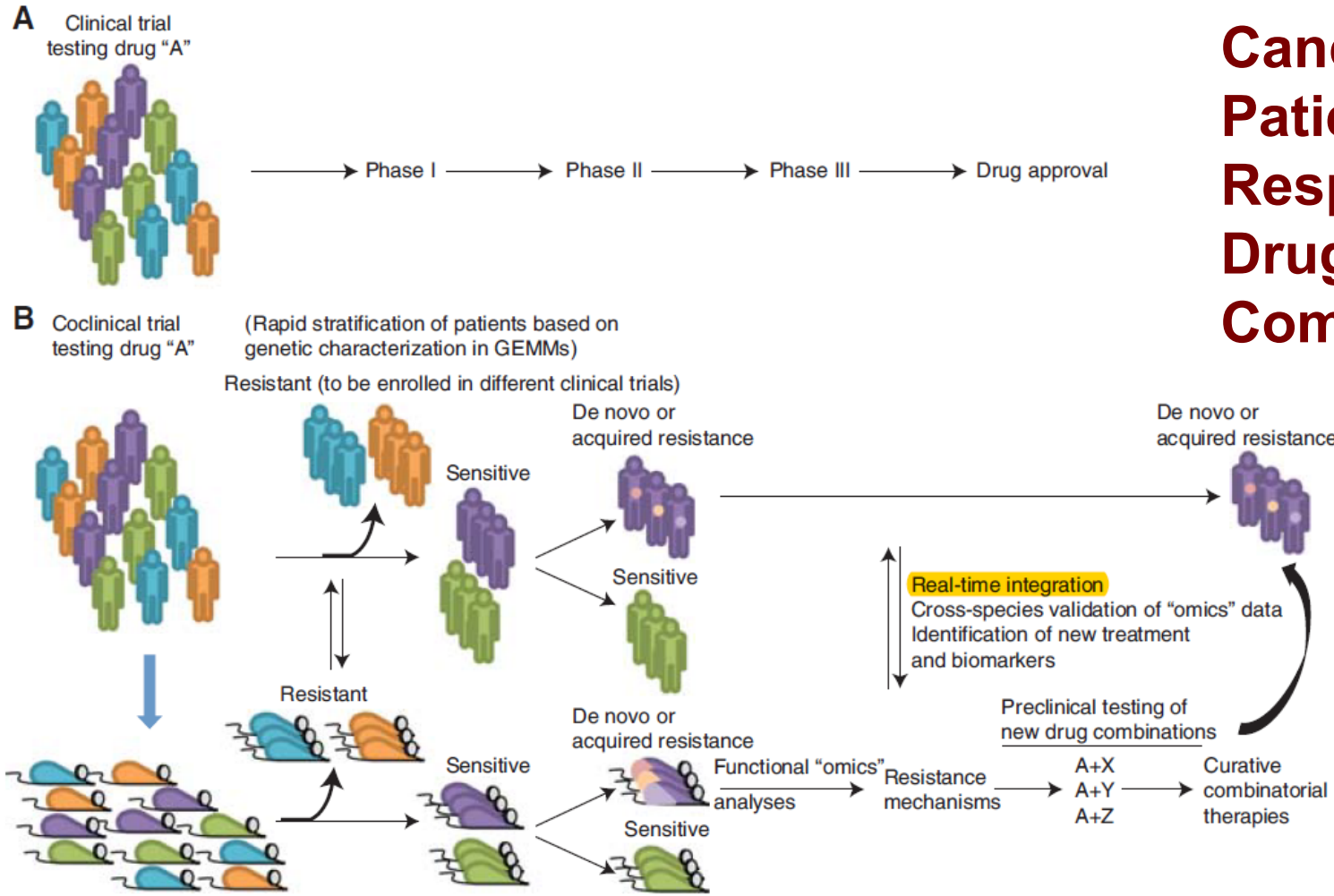
2015: NCI U24s: Co-clinical Imaging research resources, [PAR-15-266](#), [PAR-16-385](#),

2018: NCI U24s reissued: [PAR-18-841](#)

Related resources: NCI patient-Derived Models Repository, EurOPDX consortium, IMODI consortium (France), Co-clinical trials centers, mouse hospitals.

NCI initiatives: PDXnet (2017), Biological comparison of PDXs (2016),

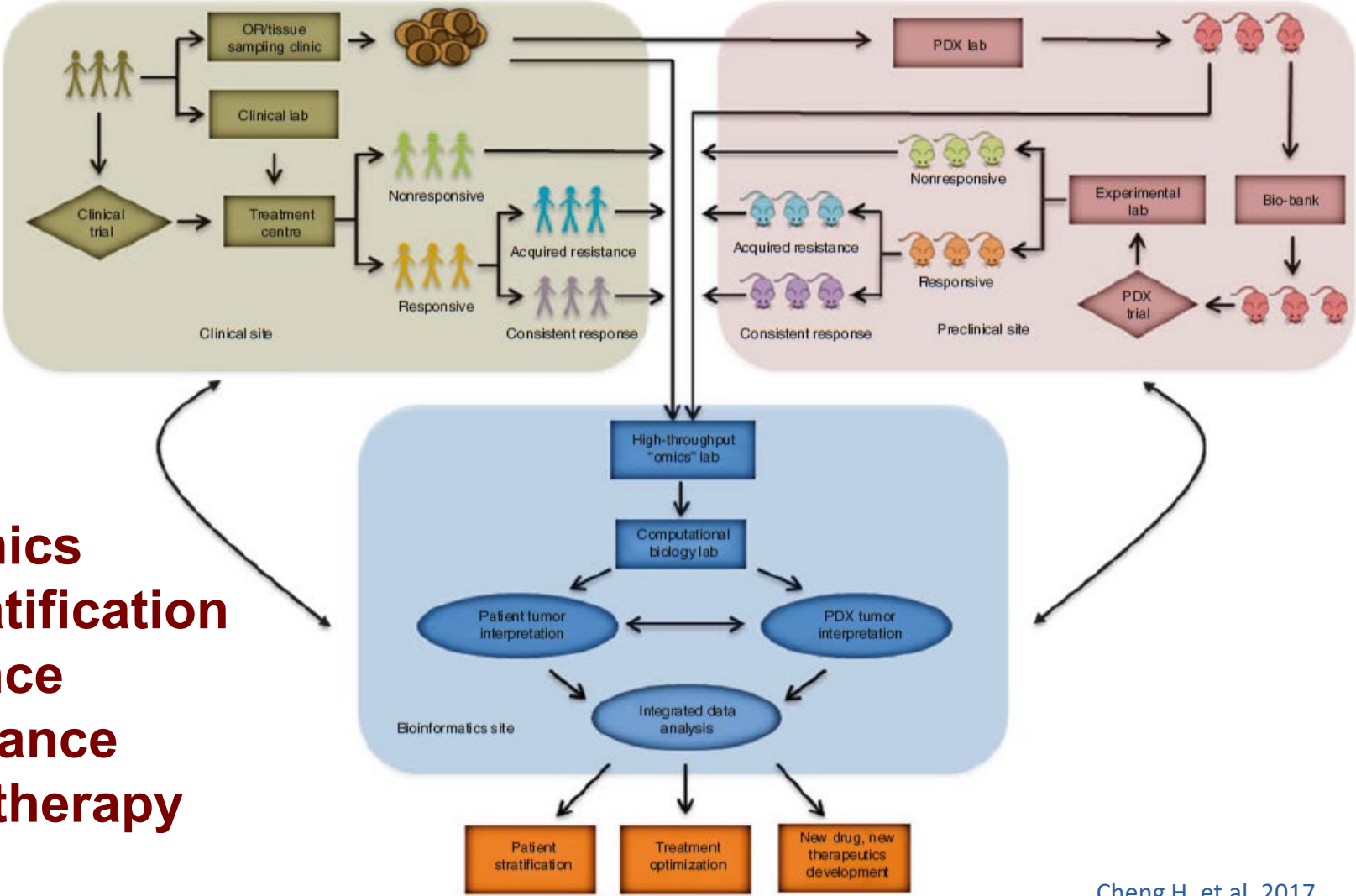
GEMMs-Based Co-Clinical Trial Platform



Cancer -omics
Patient stratification
Response
Drug resistance
Combined therapy

Chen M, et al, Code Spring Harb Perspect Med, 2017

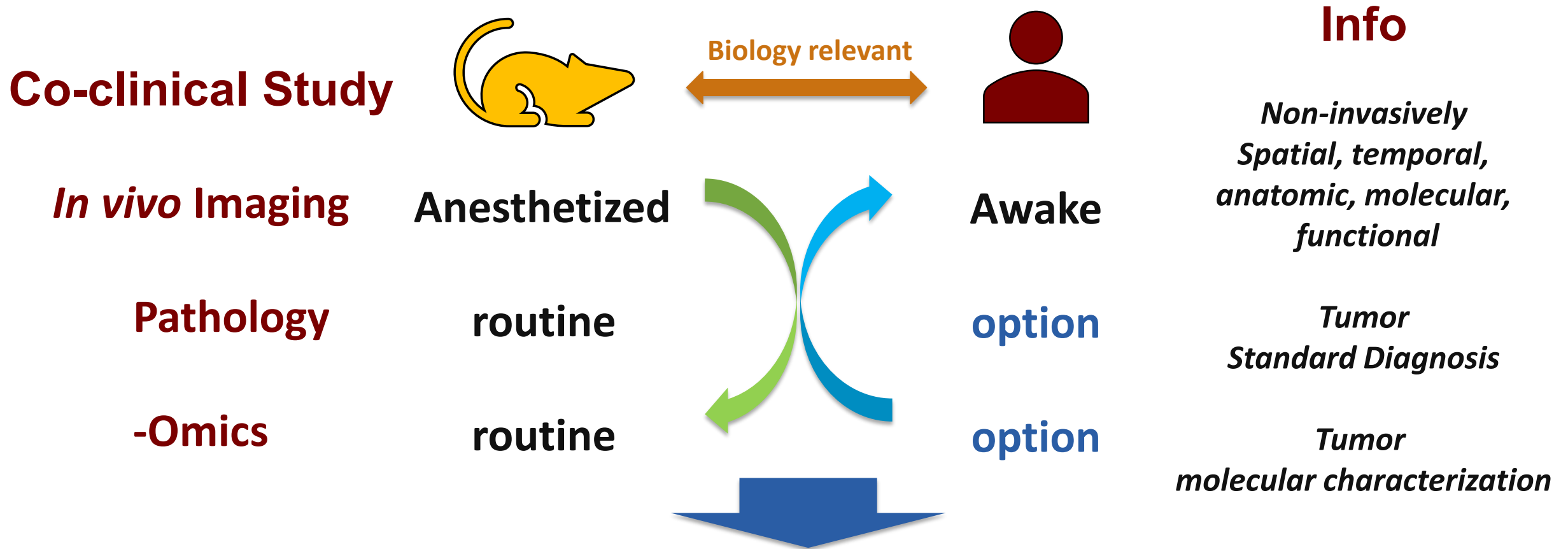
PDX-Based Co-Clinical Trial Platform



Cancer -omics
Patient stratification
Response
Drug resistance
Combined therapy

Cheng H, et al, 2017

Co-Clinical Imaging: Promise



A platform for better informing therapeutic efficacy

Co-clinical Imaging: Biology Perspective

❑ Complexity in GEMMs & PDXs:

Fidelity, Variability, Heterogeneity,
Reliability, SOPs & GLP, etc.

❑ Design of co-clinical trials:

Animal models & patients, Dosages,
Timeline for therapy & imaging

❑ Biological validations:

Histology (H&E, Immunostaining)

Genomics (WES), Transcriptomics (RNA-Seq)

Co-Clinical Imaging: Imaging Perspective

Consensus or Standardization

Clinical Imaging

Pre-clinical Imaging

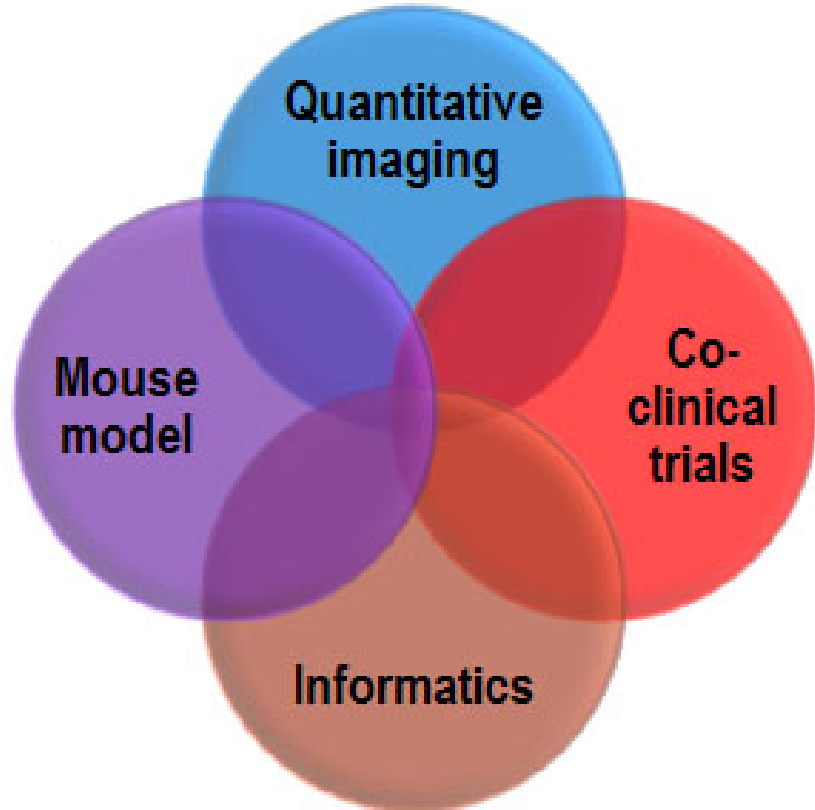
Imaging hardware	Yes	?
Imaging phantoms	MRI, PET, CT	PET (?), CT (?), MRI(?)
Imaging protocols	Quantitative	Qualitative, Semi-quantitative?
Metrology	Yes	?
Output data file formats	DICOMs	?
Data process software	Many	?
Metadata archive	Many	?
Resources	Many	?
Industry development & support	Many	?
Scientific community	SNMMI, AAPM, ISMRM, RSNA, etc.	?

PAR-18-841: Scientific Goals

Develop co-clinical imaging research resources that will encourage a consensus on how quantitative imaging (QI) methods are optimized to improve the quality of imaging results for co-clinical trials:

- ❑ Perform optimization of pre-clinical quantitative imaging methods**
- ❑ Implement optimized methods in co-clinical trials**
- ❑ Populate a web-accessible research resource with data, methods, workflow documentation, and results from co-clinical investigations.**

PAR-18-841: Required Four Elements



❑ **Co-clinical interventions:**

- Known intervention
- Therapeutic or prevention
- Prospective or retrospective

❑ **GEMMs or PDXs models:**

- Mice, available, credentialed, validated

❑ **Quantitative imaging:**

- Preclinical identical to clinic one
- New methods require IND or IDE
- User developed software tools

❑ **State-of-art informatics:**

- Encourage data integration
- Encourage use of TCIA, NCIP hub
- Encourage contribution to OMF, QIN, EDRN, etc.

PAR-18-841: Deliverable

Demonstrate the *functionality* of a web-accessible resource before the 3rd quarter of year 5 :

❑ Web-accessible functional information:

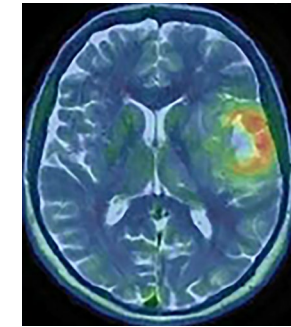
- Co-clinical imaging data
- Methods & software tools
- Workflow documentations
- Results from co-clinical investigations

❑ Demonstrating the functionality:

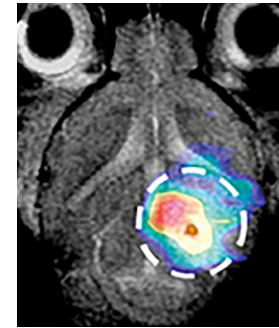
- Strategy to create the resource
- Accessibility by research community,
- Permitting research community to use and improve the proposed QI methods
- Software challenge

Available Data Expected from CIRP

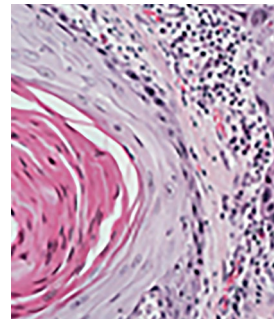
Clinical imaging



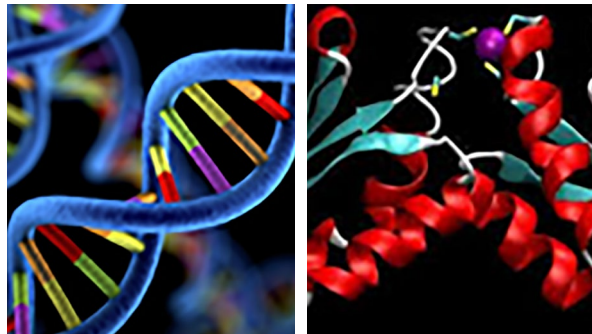
Preclinical imaging



Pathology



RNA-Seq & WES (PDXs)



Anatomical

Molecular

Correlated data sets

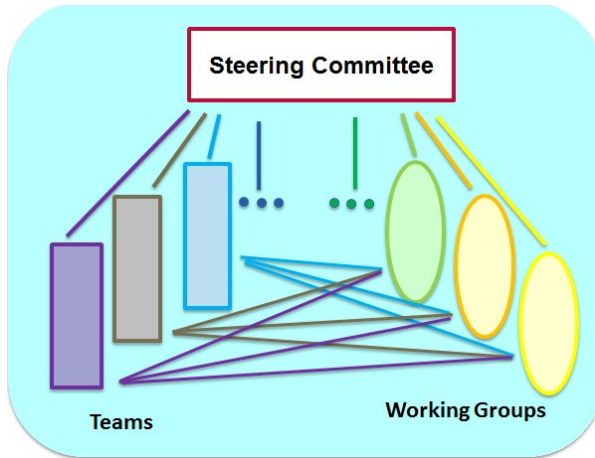
Resources provided by CIRP

- ❑ **Protocols for robust experimental design:** Animal models, biology, pathology, histopathology, imaging, QA/QC, etc.
- ❑ **Workflow for better study design & inform clinical outcome:** Workflow, methods
- ❑ **Data for data mining, metadata integration, software evaluation:** Biology, pathology, imaging
- ❑ **Software for robust, quantitative analysis:** Image processing, reconstruction, segmentation, data analysis & modeling, etc.

CIRP Network

Structure:

- ❑ **Steering Committee**
- ❑ **Three working Groups:**
 - **Animal models and co-clinical trials (AMCT)**
 - **Imaging acquisition and data process (IADP)**
 - **Informatics and outreach (IMOR)**



Activity: Open Science Approach

- ❑ **Monthly T-cons**
- ❑ **Face-to-face meeting**
- ❑ **Joint meetings with QIN and OMF**
- ❑ **Consensus documents**

CIRP Hub

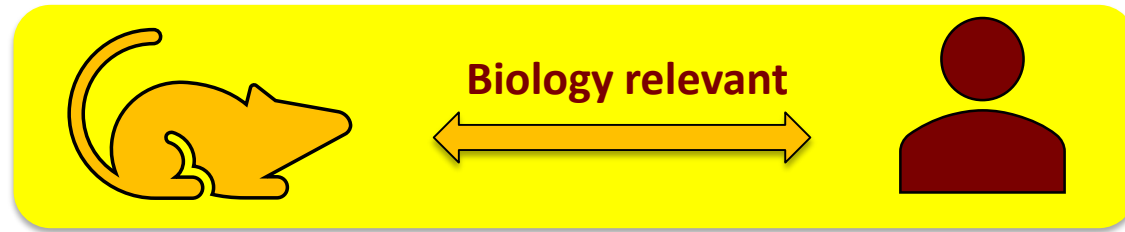
<https://nciphub.org/groups/cirphub>

The screenshot shows a web browser window displaying the CIRP Hub website. The address bar shows the URL <https://nciphub.org/groups/cirphub>. The page header includes the text "powered by NCIP Hub" and navigation links for "Login", "Register", and "Request Membership". The main title is "Co-Clinical Imaging Research Resources Program Network (CIRP) [cirphub]". Below the title is a teal navigation bar with links for "Overview", "Members", "Resources", "Forum", "Projects", "Calendar", "Announcements", "Collections", and "Activity". The "About CIRP" section contains a paragraph describing the program's goals and a list of "Four essential elements":

- Animal Models** (represented by a red icon of a mouse)
- Co-Clinical Trials** (represented by a green icon of a mouse and a person)
- Quantitative Imaging** (represented by a blue icon of a microscope)
- Informatics** (represented by a purple icon of a computer monitor with a lightning bolt)

CIRP: Standards & SOPs

Co-clinical Study



In vivo Imaging

Pre-clinical

Clinical

Pathology

routine

option

-Omics

routine

option



To be established



To be leveraged



Need development

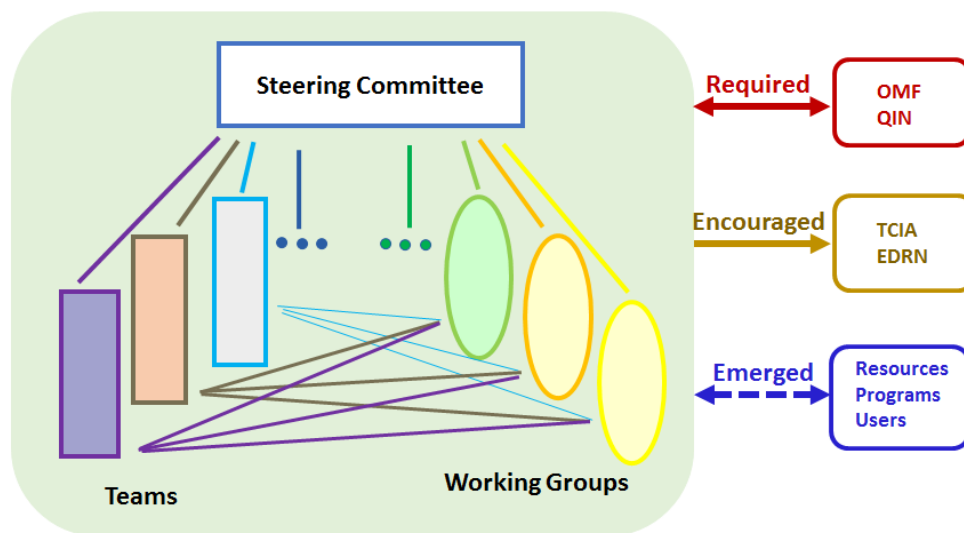
Informatics

Information archive

Metadata integration: encouraged

Outreach

- ❑ Leverage existing resources
- ❑ Ensure best practices for every CIRP element
- ❑ Address unmet need in cancer community
- ❑ Support to cancer research
- ❑ More...



Resources: Outreach & Leveraging

1. OMF: <http://oncologymodels.org/>
2. PDMC: <https://www.cancer.gov/about-nci/organization/dcb/research-programs#9>
3. PDMR: <https://pdmr.cancer.gov/models/database.htm>
4. PDXnet: <https://www.pdxnetwork.org/>
5. HTAN: <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/implementation/human-tumor-atlas>
6. SPORE: <https://trp.cancer.gov/>
7. ITCR: <https://itcr.cancer.gov/>
8. QIN:
https://imaging.cancer.gov/programs_resources/specialized_initiatives/qin/about/default.htm
9. TCIA: https://imaging.cancer.gov/informatics/cancer_imaging_archive.htm
10. GDC: <https://gdc.cancer.gov/>
11. Cancer Research Data Commons: <https://cbiit.cancer.gov/ncip/cancer-data-commons>

Summary

- ❑ Co-clinical quantitative imaging is emerging as essential non-invasive tools in cancer research
- ❑ CIRP encourages a consensus on how quantitative imaging methods are optimized to improve the quality of imaging results,
- ❑ CIRP will leverage standards or progress achieved by other existing NCI resources and programs to reaffirm best practices in every CIRP element,
- ❑ CIRP will outreach to broader cancer community to address emerging unmet needs,
- ❑ CIRP will outreach to potential users to provide better support to cancer research.



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